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A specific antibody response to HCV E2 elicited in mice by intramuscular inoculation of plasmid DNA containing coding sequences for E2.

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As the chimpanzee, the only reliable animal model for hepatitis C virus (HCV) infection, is impractical for early stage testing of HCV vaccine candidates, we have evaluated the immune response in mice to an experimental plasmid based HCV vaccine. We used this system because DNA vaccines can be rapidly constructed without the necessity of large scale protein production and purification. In this preliminary study we tested the immune response in mice to HCV envelope glycoprotein, E2, induced by a eukaryotic expression plasmid. Protein expression was monitored by immunofluorescence in transfected tissue culture cells. Each mouse was inoculated intramuscular with 100 microg plasmid DNA and some mice were boosted after 5 weeks. Among 12 BALB/C mice inoculated, 10 developed antibody to E2 by the second week. The antibody levels increased steadily before reaching a plateau in mice receiving the booster, but in the nonboosted mice the antibody declined over time. The serum from one mouse was tested against a series of overlapping peptides covering most of E2. This serum contained antibodies recognizing two distinct epitopes beginning at amino acid 57 and amino acid 113 but no antibody was directed against peptides representing the hypervariable region of E2, antibody to which is thought to be important in HCV neutralization. We have shown that the use of plasmid based vaccines can induce a specific immune response in mice against HCV antigens. This system should be useful as the first step in vaccine development.

PMID: 9021964 [PubMed - indexed for MEDLINE]